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# A facile, three-component domino protocol for the microwave-assisted synthesis of functionalized naphtho[2,3-*b*]furan-4,9-diones in water<sup>†</sup>

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A three-component domino reaction of 2-hydroxy-1,4-naphthoquinone, aromatic aldehydes and a pyridinium salt in the presence of ammonium acetate, under microwave irradiation and using water as solvent, furnished a library of novel 2-arylcarbonyl-3-aryl-4,9-dihydronaphtho-[2,3-b]furan-4,9-diones in good yields, in a transformation that presumably proceeds *via* an  $\alpha,\beta$ -unsaturated triketone generation/Michael addition/intramolecular cyclisation/air oxidation one-pot sequence.

## Introduction

The conventional multistep methods for the preparation of complex molecules involve a large number of synthetic operations, including extraction and purification processes for each individual step, that lead to synthetic inefficiency and the generation of large amounts of waste. Multicomponent reactions (MCRs) allow the creation of several bonds in a single operation and offer remarkable advantages like convergence, operational simplicity, facile automation, reduction in the number of workups, extraction and purification processes, and hence minimized waste generation rendering the transformations green. MCRs are useful for the expedient creation of chemical libraries of drug-like compounds with high levels of molecular complexity and diversity,<sup>1</sup> thereby facilitating expedient lead identification/optimization in drug discovery programmes.<sup>2</sup>

Another important aspect of green chemistry pertains to the elimination of volatile organic solvents or their replacement by non-flammable, non-volatile, non-toxic and inexpensive "green solvents".<sup>3</sup> Water complies all these stringent requirements and often exhibits important rate enhancements,<sup>4</sup> unique selectivity and reactivity.<sup>5</sup> Consequently, the development of synthetically useful reactions in water is of considerable interest.<sup>6,7</sup> In this context, the design of synthetic routes to privileged heterocyclic scaffolds of medicinal relevance that combine the synthetic efficiency of multicomponent protocols with the environmental benefits of using water as the reaction medium constitutes a very

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important challenge for green chemistry, that is only beginning to be met.<sup>8</sup>

The naphtho[2,3-*b*]furan-4,9-dione skeleton belongs to a wellknown and important class of heterocyclic quinones<sup>9</sup> prevalent in a number of natural products of biological importance (Fig. 1).<sup>10</sup> For instance, naphthofuroquinones **1–3**, isolated from *Tabebuia cassinoides*, display anticancer activity,<sup>11</sup> which has also been found in a large number of related synthetic compounds.<sup>12</sup> Kigelinone **4**, from the fruits of *Kigelia pinnata*, possesses antibacterial,<sup>13</sup> antifungal and antiviral activities,<sup>14</sup> and several synthetic naphthofuroquinones show antiprotozoal properties.<sup>15</sup> Maturone **5** and maturinone **6** are isolated from *Cacalia decomposita*, whose root extract has been used for the treatment of diabetes.<sup>16</sup> Naphthofuroquinones have also been identified as components of medicinal preparations widely used in North and South America.



Fig. 1 Some natural, bioactive naphtho[2,3-b]furan-4,9-diones.

The first naphtho[2,3-*b*]furan-4,9-dione was synthesised from 2-hydroxy-1,4-naphthoquinone *via* a multistep approach.<sup>17</sup> More recent methods include [3 + 2]-cycloaddition-based protocols involving C- and O-alkylations of naphthoquinones by 1,

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3-dicarbonyl compounds,<sup>18</sup> CAN-promoted oxidative reactions<sup>19</sup> or [3 + 2] photoadditions,<sup>20</sup> Pd- or Cu-catalysed sequential coupling/annulation,<sup>21</sup> tandem O-Michael-carbene insertion,<sup>22</sup> condensation-[4 + 1]cycloaddition or [3 + 1 + 1]furoannulation<sup>23</sup> and a number of multistep strategies.<sup>24</sup> Most of these are multistep protocols, that suffer from generation of by-products, low yields and use of metal-containing reagents. Therefore, efficient new synthetic methods employing non-toxic reagents and solvents are highly desirable from the viewpoint of green chemistry. We describe in this paper our findings on the synthesis of functionalized naphtho[2,3-*b*]furan-4,9-diones using a three-component domino protocol in water.

#### **Results and discussion**

As shown in Scheme 1 and Table 1, we started our study with the optimization of the three-component reaction between 2-hydroxy-1,4-naphthoquinone 7 (1 mmol), benzaldehyde **8a** (1 mmol) and 1-(2-oxo-2-phenylethyl)pyridinium bromide **9** (1 mmol) in the presence of ammonium acetate (5 mmol) in acetonitrile under reflux for 10 h, which afforded 2-benzoyl-3-phenyl-4,9-dihydronaphtho[2,3-*b*]furan-4,9-dione **10a** in 68% yield (Fig. 2).



Scheme 1 Synthesis of 2-aroyl-3-arylnaphtho[2,3-*b*]furan-4,9-diones 10.

Because of the advantages of the use of microwave irradiation,<sup>25,26</sup> we also studied this model reaction under focused microwave irradiation in sealed vessels at 130 °C and 150 W for 20 min, and obtained **10a** in 79% yield (entry 1, Table 1), which encouraged us to carry out all our subsequent studies

 Table 1
 Solvent- and base-screen for the synthesis of compound 10a

 under microwave irradiation

Entry	Base	Solvent	Time, min	Yield,%"
1	NH <sub>4</sub> OAc	CH <sub>3</sub> CN	20	79
2	NH₄OAc	DMF	25	41
3	NH₄OAc	MeOH	25	57
4	NH₄OAc	EtOH	20	63
5	NH₄OAc	Ethylene glycol	25	74
6	NH₄OAc	Water	20	86
7	NaOAc	Water	20	59
8	$K_2CO_3$	Water	20	47
9	Et <sub>3</sub> N	Water	25	32
10	Et <sub>2</sub> NH	Water	25	42
11	L-Proline	Water	20	0 <sup>b</sup>
12	Morpholine	Water	20	$0^{b}$

<sup>*a*</sup> Isolated yield after purification. A 68% yield was obtained after 10 h in refluxing acetonitrile. <sup>*b*</sup> No reaction was found.



Fig. 2 Structure of compound 10a obtained during optimization studies.

under microwave irradiation, using the previously mentioned conditions. We were also encouraged to undertake this study by the fact that the use of microwave irradiation in sealed vessels has been proven to be accompanied by energy savings, probably associated mainly to the shortened reaction time,<sup>27</sup> although it has been recently shown that improvements in energy efficiency are significant only for industrial-scale applications involving multimode reactors.<sup>28</sup> In search for a greener solvent, the reaction was performed in N,N-dimethylformamide (DMF), methanol, ethanol, ethylene glycol and water (entries 2-6). Gratifyingly, we found that the reaction in water furnished the maximum yield of the product (86%) in only 20 min (entry 6), and hence all subsequent experiments were performed in this medium. The model reaction was also investigated employing different bases, viz. sodium acetate, potassium carbonate, triethylamine, diethylamine, L-proline and morpholine (entries 7-12), and the results show that the initial ammonium acetatewater combination was ideal for the reaction. To the best of our knowledge, domino reactions employing pyridinium ylides generated in situ for the construction of 2-aroyl-3-aryl-4,9dihydronaphtho[2,3-b]furan-4,9-diones in water medium have not been reported yet.

Having established the optimal conditions, we explored the scope and generality of the method by preparing a library of hitherto unreported 2-aroyl-3-aryl-4,9-dihydronaphtho[2,3-b]furan-4,9-diones **10** (Scheme 1 and Table 2). Typically, a mixture of 2-hydroxy-1,4-naphthoquinone **7**, aromatic aldehyde **8**, 1-(2-oxo-2-arylethyl)pyridinium bromide **9** and NH<sub>4</sub>OAc (1:1:1:5 mmol) in a sealed vial was irradiated in a focused microwave oven at 130 °C and 150 W for 20 min. After

 Table 2
 Synthesis of compounds 10: comparison between conventional and microwave-assisted reactions

				Yield (%) <sup>a</sup>	
Entry	Compound	Ar	$Ar^1$	Thermal	Microwave
1	10a	C <sub>6</sub> H <sub>5</sub>	C <sub>6</sub> H <sub>5</sub>	73	86
2	10b	4-MeC <sub>6</sub> H <sub>4</sub>	$C_6H_5$	73	80
3	10c	$4-ClC_6H_4$	$C_6H_5$	74	82
4	10d	$4-FC_6H_4$	$C_6H_5$	75	81
5	10e	$4-O_2NC_6H_4$	$C_6H_5$	81	86
6	10f	$C_6H_5$	$4-ClC_6H_4$	74	76
7	10g	$4-Pr^{i}C_{6}H_{4}$	$4-ClC_6H_4$	66	74
8	10h	$4-ClC_6H_4$	$4-ClC_6H_4$	80	84
9	10i	$4-FC_6H_4$	$4-ClC_6H_4$	71	79
10	10j	$4-ClC_6H_4$	4-MeC <sub>6</sub> H <sub>4</sub>	75	80
11	10k	$4-FC_6H_4$	4-MeC <sub>6</sub> H <sub>4</sub>	68	77
12	101	$C_6H_5$	2-Naphthyl	77	83
13	10m	4- <sup>i</sup> PrC <sub>6</sub> H <sub>4</sub>	2-Naphthyl	70	78
14	10n	$4-ClC_6H_4$	2-Naphthyl	74	81
15	100	$3-FC_6H_4$	2-Naphthyl	71	77

" Isolated yield after purification.

completion of the reaction (TLC), the products 10 were isolated and purified by simple filtration through a pad of silica gel. For comparison purposes, the reactions were also performed at 100 °C in water for 10 h. Although the overall yields obtained for both cases can be considered excellent bearing in mind the large number of steps involved in the domino sequence, the yield of the reaction was consistently enhanced under microwave irradiation (74-86%, compared to 66-81% under conventional heating conditions). Other advantages of the microwave-promoted conditions include the dramatically shorter reaction time and lower energy requirements. Thus, the energy efficiency of both sets of conditions was studied for the synthesis of compound 10a, for which the energy consumption under microwave-assisted and thermal conditions was determined experimentally by using a watt-meter and found to be ca. eight times lower for the former (0.13 kWh vs. 1.03 kWh).

The structures of the naphtho[2,3-*b*]furan-4,9-diones **10a–100** were fully characterized by <sup>1</sup>H and <sup>13</sup>C NMR, IR and mass spectroscopic data and elemental analysis. For example, in the <sup>1</sup>H NMR spectrum of **10b**, the H-3' and H-2' showed two doublets with J = 8.1 Hz at 7.21 and 7.40 ppm (Fig. 3). The H-3",5" showed a triplet at 7.43 ppm (J = 7.8 Hz), whilst the H-2",6" appeared as a doublet of doublets at 7.92 ppm (J = 8.1 and 1.2 Hz). The H-4" appeared as a multiplet at 7.55–7.60 ppm. The multiplet in the chemical shift range of 7.79–7.82 ppm is assigned to H-6 and H-7. The H-5 and H-8 showed multiplets at 8.16–8.19 ppm and 8.26–8.29 ppm in view of their proximity to the adjacent carbonyl groups. The chemical shifts of the hydrogens and the respective C,H-COSY correlations allowed to assign the connected carbon chemical shifts (Fig. 3).

A plausible mechanism for the formation of naphtho[2,3b]-furan-4,9-diones 10 is depicted in Scheme 2. Presumably, the intermediate 3-[1-arylmethylidene]-1,2,3,4-tetrahydro-1,2,4naphthalenetriones 14 could arise in two ways: (i) *via* the Mannich reaction of 2-hydroxy-1,4-naphthoquinone 7 with an iminium ion 11 generated from 8 and ammonium acetate, followed by elimination of ammonia, or (ii) the ammonium acetate-catalyzed reaction of 7 with the starting aldehyde to afford aldol 13, which would undergo dehydration. The mechanism involving an iminium ion presumably explains the higher yield obtained in presence of ammonium acetate than



**Fig. 3** <sup>1</sup>H and <sup>13</sup>C NMR assignment in compound **10b**, as a representative example.

with other catalysts. Then, the Michael addition of pyridinium ylide **15** (generated *in situ* from **9**) to **14** presumably affords the pyridinium enolate **16**, which subsequently undergoes annulation *via* displacement of pyridine to give **17**, which is probably in tautomeric equilibrium with the corresponding hydroquinone **18**. Ultimately, these intermediates are transformed into the final products **10** *via* air oxidation. Overall, this three-component domino transformation leads to the generation of one C–O and two C–C bonds.

### Conclusions

In conclusion, a facile one-pot, three-component reaction for the efficient assembly of naphtho[2,3-*b*]furan-4,9-diones, structurally related to medicinally important compounds, *via* an aldol (Mannich)/Michael addition/annulation *via* nucleophilic displacement/air oxidation domino sequence in water is described. The present work constitutes the first report of the synthesis of dihydrofurans employing the enol form of a triketone, *viz*. 2-hydroxy-1,4-naphthoquinone with pyridinium ylide generated *in situ* from the reaction of phenacylpyridinium salt.<sup>29</sup> Furthermore, our protocol employs focused microwave irradiation and water as a green solvent.

#### Experimental

Melting points were measured in open capillary tubes and are uncorrected. A CEM Discover microwave synthesizer (Model



Scheme 2 Probable domino sequence leading to the formation of 10.

No: 908010) operating at 180/264 V and 50/60 Hz with microwave power maximum level of 300 W and microwave frequency of 2455 MHz was employed for the microwaveassisted experiments done in this work. The <sup>1</sup>H NMR, <sup>13</sup>C NMR and C,H-COSY spectra were recorded on a Bruker (Avance) 300 MHz NMR instrument using TMS as internal standard and CDCl<sub>3</sub> as solvent. Standard Bruker software was used throughout. Chemical shifts are given in parts per million ( $\delta$ scale) and the coupling constants are given in Hertz. Silica gel-G plates (Merck) were used for TLC analysis with a mixture of petroleum ether (60-80 °C) and ethyl acetate as eluent. Elemental analyses were performed on a Perkin Elmer 2400 Series II Elemental CHNS analyzer. IR spectra were recorded on a JASCO FT IR instument (KBr pellet method). HRMS measurements were performed by the CAI de Espectrometria de Mass, Universidad Complutense, using an FTMS Bruker APEX QIV instrument. Energy consumption for thermal and microwave irradiation reactions have been determined using a wattmeter manufactured by H. Brennenstuhl GmbH & Co. KG-D-72074 Tubingen (Model PM 240 S-D, 230V AC-50 Hz max. 16A/3680W).

#### General procedure for synthesis of naphtho[2,3-*b*]-furane-4,9dione derivatives 10

**Conventional heating method.** A mixture of 2-hydroxy-1,4naphthoquinone 7 (0.300 g, 1.72 mmol), the suitable aromatic aldehyde (1.72 mmol), 1-(2-oxo-2-phenylethyl)pyridinium bromide 9 (0.479 g, 1.72 mmol), and NH<sub>4</sub>OAc (0.663 g, 8.6 mmol) in water (10 mL) was refluxed in an oil bath for 10 h. After completion of the reaction (TLC), the product was extracted with ethyl acetate (10 ml) and purified by filtration through a pad of silica gel using a 3 : 1 AcOEt-petroleum ether mixture, to yield pure **10**.

Microwave irradiation method. A vial containing a mixture of 2-hydroxy-1,4-naphthoquinone 7 (0.300 g, 1.72 mmol), aromatic aldehyde (1.72 mmol), 1-(2-oxo-2-phenylethyl)pyridinium bromide 9 (0.479 g, 1.72 mmol), and NH<sub>4</sub>OAc (0.663 g, 8.60 mmol) in water (7 ml) was sealed and placed in a CEM Discover microwave oven. The vial was subjected to microwave irradiation, programmed at 130 °C and 150 W. After a period of 3–5 min, the temperature reached a plateau, 130 °C, and remained constant. After completion of the reaction (20 min), the vial was cooled to room temperature and extracted with ethyl acetate (10 ml) and purified by filtration through a pad of silica gel using a 3:1 AcOEt–petroleum ether mixture, to yield pure 10. Characterization data of all compounds are given below.

**2-Benzoyl-3-phenyl-4,9-dihydronaphtho**[**2**,**3**-*b*]**furane-4,9-dione (10a).** Yellow solid; Yield: 86% (MW), 73% (Thermal); m.p. 137–138 °C; IR (KBr): 1681, 1587, 1436, 1357, 1322 cm<sup>-1</sup>; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta_{\text{H}}$ : 7.32-7.34 (m, 4H, Ar–H), 7.40-7.43 (m, 2H, Ar–H), 7.48 (t, 2H, Ar–H), 7.71-7.74 (m, 2H, Ar–H), 7.82 (d, 2H, J = 7.8 Hz, Ar–H), 8.08-8.11 (m, 1H, Ar–H), 8.18-8.21 (m, 1H, Ar–H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta_{\text{C}}$ : 126.8, 127.2, 127.7, 127.8, 128.2, 128.4, 129.0, 129.8, 130.1, 131.7, 132.3, 133.5, 133.7, 133.9, 134.4, 136.0, 150.5, 152.3, 173.9, 179.8, 183.6. HRMS (negative ESI): m/z calcd for C<sub>25</sub>H<sub>14</sub>O<sub>4</sub>, 378.08921. Found: 378.08976. Anal. calcd for  $C_{25}H_{14}O_4$ : C, 79.36; H, 3.73%. Found: C, 79.29; H, 3.66%.

**2-Benzoyl-3-(4-methylphenyl)-4,9-dihydronaphtho**[**2**,3-*b*]**furane-4,9-dione (10b).** Yellow solid; Yield: 80% (MW), 73% (Thermal); m.p. 154–155 °C; IR (KBr): 1681, 1621, 1348, 1267 cm<sup>-1</sup>; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta_{\rm H}$ : 2.41 (s, 3H, CH<sub>3</sub>), 7.21 (d, 2H, J = 8.1 Hz, Ar–H), 7.40 (d, 2H, J = 8.1 Hz, Ar–H), 7.44(d, 2H, J = 7.8 Hz, Ar–H), 7.54–7.59 (m, 1H, Ar–H), 7.78–7.81 (m, 2H, Ar–H), 7.92 (dd, 2H, J = 8.4, 1.2 Hz, Ar–H), 8.16–8.19 (m, 1H, Ar–H), 8.25–8.28 (m, 1H, Ar–H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta_{\rm C}$ : 21.3, 125.1, 126.8, 127.2, 127.8, 128.4, 128.6, 129.8, 130.0, 132.0, 132.3, 133.5, 133.8, 133.9, 134.3, 136.0, 139.1, 150.4, 152.3, 174.0, 179.8, 183.7. HRMS (positive ESI): m/z calcd for C<sub>26</sub>H<sub>16</sub>O<sub>4</sub> + Na<sup>+</sup>: 415.09463. Found: 415.09408. Anal. calcd for C<sub>26</sub>H<sub>16</sub>O<sub>4</sub>: C, 79.58; H, 4.11%. Found: C, 79.50; H, 4.05%.

**2-Benzoyl-3-(4-chlorophenyl)-4,9-dihydronaphtho**[**2**,3-*b*]**furane-4,9-dione (10c).** Yellow solid; Yield: 82% (MW), 74% (Thermal); m.p. 242–243 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta_{\rm H}$ : 7.37 (d, 2H, *J* = 8.7 Hz, Ar–H), 7.43–7.48 (m, 4H, Ar–H), 7.57–7.63 (m, 1H, Ar–H), 7.74–7.83 (m, 2H, Ar–H), 7.92 (d, 2H, *J* = 8.7 Hz, Ar–H), 8.13–8.18 (m, 1H, Ar–H), 8.24–8.29 (m, 1H, Ar–H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta_{\rm C}$ : 126.6, 126.9, 127.3, 127.6, 128.1, 128.6, 129.8, 130.7, 131.5, 132.2, 133.6, 133.7, 134.1, 134.5, 135.3, 135.8, 150.5, 152.3, 173.8, 179.8, 183.4. HRMS (positive ESI): *m*/*z* calcd for C<sub>25</sub>H<sub>13</sub>ClO<sub>4</sub> + Na<sup>+</sup>: 435.04001 (M<sup>+</sup>) and 437.03706 (M + 2)<sup>+</sup>. Found: 435.03946 and 437.03651. Anal. calcd for C<sub>25</sub>H<sub>13</sub>ClO<sub>4</sub>: C, 72.74; H, 3.17%. Found: C, 72.66; H, 3.11%.

**2-Benzoyl-3-(4-fluorophenyl)-4,9-dihydronaphtho**[**2**,3-*b*]furane-**4**,9-dione (10d). Yellow solid; Yield: 81% (MW), 75% (Thermal); m.p. 166–167 °C; IR (KBr): 1741, 1677, 1646, 1486, 1442 cm<sup>-1</sup>; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta_{\rm H}$ : 7.06–7.12 (m, 1H, Ar–H), 7.26–7.30 (m, 1H, Ar–H), 7.42–7.53 (m, 4H, Ar–H), 7.57–7.62 (m, 1H, Ar–H), 7.80–7.84 (m, 2H, Ar–H), 7.92 (d, 2H, J = 8.4 Hz, Ar–H), 8.17–8.20 (m, 1H, Ar–H), 8.26–8.31 (m, 1H, Ar–H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta_{\rm C}$ : 115.6, 124.1, 126.9, 127.3, 127.7, 128.6, 129.9, 130.2, 131.0, 132.3, 133.8, 134.1, 134.2, 134.5, 136.0, 150.6, 152.4, 163.3, 174.0, 180.0, 183.6. HRMS (positive ESI): m/z calcd for C<sub>25</sub>H<sub>13</sub>FO<sub>4</sub> + Na<sup>+</sup>: 419.06956. Found: 419.06901. Anal. calcd for C<sub>25</sub>H<sub>13</sub>FO<sub>4</sub>: C, 75.75; H, 3.31%. Found: C, 75.68; H, 3.37%.

**2-Benzoyl-3-(4-nitrophenyl)-4,9-dihydronaphtho**[**2**,3-*b*]furane-**4,9-dione (10e).** Yellow solid; Yield: 86% (MW), 81% (Thermal); m.p. 237–238 °C; IR (KBr): 1679, 1671, 1654, 1348, 1230 cm<sup>-1</sup>; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta_{\rm H}$ : 7.50 (t, 2H, *J* = 7.5 Hz, Ar–H), 7.64 (t, 1H, *J* = 7.5 Hz, Ar–H), 7.70 (d, 2H, *J* = 8.7 Hz, Ar–H), 7.82–7.85 (m, 2H, Ar–H), 8.00 (d, 2H, *J* = 7.2 Hz, Ar–H), 8.16–8.18 (m, 1H, Ar–H), 8.28–8.31 (m, 3H, Ar–H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta_{\rm C}$ : 123.1, 127.1, 127.4, 127.7, 128.8, 129.8, 130.0, 131.3, 132.3, 133.6, 134.2, 134.4, 134.7, 135.3, 135.7, 148.2, 150.9, 152.4, 173.8, 179.8, 183.1. HRMS (positive ESI): *m/z* calcd for C<sub>25</sub>H<sub>13</sub>NO<sub>6</sub> + Na<sup>+</sup>: 446.06406. Found: 446.06351. Anal. calcd for C<sub>25</sub>H<sub>13</sub>NO<sub>6</sub>: C, 70.92; H, 3.09; N, 3.31%. Found: C, 70.86; H, 3.02; N, 3.25%. **2-(4-Chlorobenzoyl)-3-phenyl-4,9-dihydronaphtho[2,3-***b***]furane-4,9-dione (10f). Yellow solid; Yield: 76% (MW), 74% (Thermal); m.p. 208–209 °C; IR (KBr): 1743, 1691, 1529, 1295 cm<sup>-1</sup>; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) \delta\_{\rm H}: 7.26 (s, 1H, Ar–H), 7.40 (d, 2H, J = 8.7 Hz, Ar–H), 7.42–7.43 (m, 2H, Ar–H), 7.47– 7.50 (m, 2H, Ar–H), 7.79–7.82 (m, 2H, Ar–H), 7.87 (d, 2H, J = 8.7 Hz, Ar–H), 8.16–8.19 (m, 1H, Ar–H), 8.26–8.29 (m, 1H, Ar–H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) \delta\_{\rm C}: 126.8, 127.3, 127.7, 127.9, 128.0, 128.8, 129.2, 130.1, 131.2, 132.2, 133.7, 134.0, 134.3, 134.4, 140.2, 150.1, 152.4, 173.9, 179.7, 182.2. HRMS (positive ESI): m/z calcd for C<sub>25</sub>H<sub>13</sub>ClO<sub>4</sub> + Na<sup>+</sup>: 435.04001 (M<sup>+</sup>) and 437.03706 (M + 2)<sup>+</sup>. Found: 435.03946 and 437.03651. Anal. calcd for C<sub>25</sub>H<sub>13</sub>ClO<sub>4</sub>: C, 72.74; H, 3.17%. Found: C, 72.66; H, 3.21%.** 

**2-(4-Chlorobenzoyl)-3-(4-isopropylphenyl)-4,9-dihydro naphtho[2,3-***b***]<b>furane-4,9-dione (10g).** Yellow solid; Yield: 74% (MW), 66% (Thermal); m.p. 188–189 °C; IR (KBr): 1679, 1658, 1589, 1357, 1326 cm<sup>-1</sup>; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta_{\rm H}$ : 1.27 (d, 6H, J = 6.9 Hz, CH<sub>3</sub>), 2.89–3.00 (m, 1H, CH), 7.21 (d, 2H, J = 9.0 Hz, Ar–H), 7.32–7.39 (m, 4H, Ar–H), 7.76–7.82 (m, 4H, Ar–H), 8.17–8.20 (m, 1H, Ar–H), 8.26–8.29 (m, 1H, Ar–H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta_{\rm C}$ : 23.8, 34.0, 125.2, 126.0, 126.9, 127.4, 127.8, 128.8, 130.3, 131.2, 132.3, 132.5, 133.9, 134.0, 134.5, 140.0, 150.2, 150.3, 152.7, 174.0, 179.9, 182.6. HRMS (positive ESI): m/z calcd for C<sub>28</sub>H<sub>19</sub>ClO<sub>4</sub> + Na<sup>+</sup>: 477.08696 (M<sup>+</sup>) and 479.08401 (M<sup>+</sup> + 2). Found: 477.08641 and 479.08346. Anal. calcd for C<sub>28</sub>H<sub>19</sub>ClO<sub>4</sub>: C, 73.93; H, 4.21%. Found: C, 73.87; H, 4.14%.

**2-(4-Chlorobenzoyl)-3-(4-chlorophenyl)-4,9-dihydronaphtho-[2,3-b]furan-4,9-dione (10h).** Yellow solid; Yield: 84% (MW), 80% (Thermal); m.p. 246–247 °C; IR (KBr): 1683, 1689, 1527, 1348, 1299 cm<sup>-1</sup>; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta_{\rm H}$ : 7.26–7.29 (m, 1H, Ar–H), 7.40–7.49 (m, 5H, Ar–H), 7.80–7.83 (m, 2H, Ar–H), 7.93 (d, 2H, J = 8.7 Hz, Ar–H), 8.16–8.19 (m, 1H, Ar–H), 8.26–8.30 (m, 1H, Ar–H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta_{\rm C}$ : 126.4, 126.9, 127.3, 127.6, 128.2, 128.8, 129.0, 131.2, 131.5, 132.2, 133.6, 134.1, 134.6, 135.5, 140.5, 150.1, 152.3, 173.9, 179.7, 182.0. HRMS (positive ESI): m/z calcd for C<sub>25</sub>H<sub>12</sub>Cl<sub>2</sub>O<sub>4</sub> + Na<sup>+</sup>: 469.00103 (M<sup>+</sup>), 470.99808 (M + 2)<sup>+</sup>, 473.00479 (M + 4)<sup>+</sup>. Found: 469.00049, 470.99754, 472.99463. Anal. calcd for C<sub>25</sub>H<sub>12</sub>Cl<sub>2</sub>O<sub>4</sub>: C, 67.13; H, 2.70%. Found: C, 67.05; H, 2.64%.

**2-(4-Chlorobenzoyl)-3-(4-fluorophenyl)-4,9-dihydronaphtho-[2,3-b]furane-4,9-dione (10i).** Yellow solid; Yield: 79% (MW), 71% (Thermal); m.p. 221–222 °C; IR (KBr): 1684, 1643, 1531, 1351, 1224 cm<sup>-1</sup>; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta_{\rm H}$ : 7.10–7.17 (m, 2H, Ar–H), 7.43–7.47 (m, 2H, Ar–H), 7.49–7.55 (m, 2H, Ar–H), 7.80–7.84 (m, 2H, Ar–H), 7.89–7.93 (m, 2H, Ar–H), 8.16–8.20 (m, 1H, Ar–H), 8.26–8.30 (m, 1H, Ar–H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta_{\rm C}$ : 115.6, 124.0, 127.0, 127.4, 127.7, 129.0, 131.3, 131.5, 132.2, 133.8, 134.2, 134.3, 134.6, 140.5, 150.2, 152.4, 163.3, 173.9, 179.8, 182.2. HRMS (positive ESI): *m/z* calcd for C<sub>25</sub>H<sub>12</sub>CIFO<sub>4</sub> + Na<sup>+</sup>: 453.03058 (M<sup>+</sup>), 455.02763 (M + 2)<sup>+</sup>. Found: 453.03004, 455.02709. Anal. calcd for C<sub>25</sub>H<sub>12</sub>CIFO<sub>4</sub>: C, 69.70; H, 2.81%. Found: C, 69.63; H, 2.86%.

**3-(4-Chlorophenyl)-2-(4-methylbenzoyl)-4,9-dihydro naphtho-**[2,3-b]furane-4,9-dione (10j). Yellow solid; Yield: 80% (MW), 75% (Thermal); m.p. 253–254 °C; IR (KBr): 1679, 1641, 1590, 1355, 1218 cm<sup>-1</sup>; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta_{\rm H}$ : 2.43 (s, 3H, CH<sub>3</sub>), 7.25–7.28 (m, 2H, Ar–H), 7.39 (d, 2H, *J* = 8.7 Hz, Ar–H), 7.47 (d, 2H, *J* = 8.7 Hz, Ar–H), 7.79–7.81 (m, 2H, Ar–H), 7.85 (d, 2H, *J* = 8.4 Hz, Ar–H), 8.16–8.19 (m, 1H, Ar–H), 8.26–8.29 (m, 1H, Ar–H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta_{\rm C}$ : 21.7, 126.8, 126.9, 127.2, 127.3, 127.7, 128.2, 129.4, 129.6, 129.9, 130.1, 130.4, 131.6, 132.3, 133.4, 133.8, 134.1, 134.5, 135.3, 145.1, 150.9, 152.3, 173.9, 179.9,183.1. HRMS (positive ESI): *m/z* calcd for C<sub>26</sub>H<sub>15</sub>ClO<sub>4</sub> + Na<sup>+</sup>: 449.05566 (M<sup>+</sup>), 451.05271 (M + 2)<sup>+</sup>. Found: 449.05511, 451.05216. Anal. calcd for C<sub>26</sub>H<sub>15</sub>ClO<sub>4</sub>: C, 73.16; H, 3.54%. Found: C, 73.09; H, 3.48%.

**3-(4-Fluorophenyl)-2-(4-methylbenzoyl)-4,9-dihydronaphtho-[2,3-b]furane-4,9-dione (10k).** Yellow solid; Yield: 77% (MW), 68% (Thermal); m.p. 231–232 °C;  $v_{max}$ (KBr): 1756, 1683, 1621, 1348, 1295 cm<sup>-1</sup>; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta_{\rm H}$ : 7.02–7.08 (m, 2H, Ar–H), 7.19–7.21 (m, 2H, Ar–H), 7.44–7.49 (m, 2H, Ar–H), 7.74–7.77 (m, 2H, Ar–H), 7.79 (d, 2H, J = 8.1 Hz), 8.11–8.14 (m, 1H, Ar–H), 8.21–8.24 (m, 1H, Ar–H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta_{\rm C}$ : 21.7, 115.0, 124.2, 124.3, 126.9, 127.3, 127.7, 129.3, 130.1, 130.5, 132.2, 133.4, 133.8, 134.1, 134.5, 145.0, 150.9, 152.3, 164.7, 174.0, 180.0, 183.2. HRMS (positive ESI): m/z calcd for C<sub>26</sub>H<sub>15</sub>FO<sub>4</sub> + Na<sup>+</sup>: 433.08521 (M<sup>+</sup>). Found: 433.08466. Anal. calcd for C<sub>26</sub>H<sub>15</sub>FO<sub>4</sub>: C, 76.09; H, 3.68%. Found: C, 76.02; H, 3.60%.

**2-(2-Naphthylcarbonyl)-3-phenyl-4,9-dihydronaphtho**[2,3-*b*]furane-4,9-dione (10l). Yellow solid; Yield: 83% (MW), 77% (Thermal); m.p. 233–234 °C; IR (KBr): 1670, 1665, 1587, 1357, 1267 cm<sup>-1</sup>; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta_{\rm H}$ : 7.23–7.27 (m, 2H, Ar–H), 7.33–7.37 (m, 2H, Ar–H), 7.52–7.65 (m, 3H, Ar–H), 7.80–7.85 (m, 3H, Ar–H), 7.88–7.98 (m, 3H, Ar–H), 8.19–8.21 (m, 1H, Ar–H), 8.28–8.29 (m, 1H, Ar–H), 8.45 (s, 1H, Ar– H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta_{\rm C}$ : 124.7, 126.8, 126.9, 127.3, 127.8, 127.9, 128.3, 128.5, 129.0, 129.1, 129.8, 130.2, 131.7, 132.3, 132.4, 132.6, 133.3, 133.9, 134.0, 134.4, 135.8, 150.9, 152.5, 174.0, 179.9, 183.6. HRMS (positive ESI): *m/z* calcd for C<sub>29</sub>H<sub>16</sub>O<sub>4</sub> + Na<sup>+</sup>: 451.09463 (M<sup>+</sup>). Found: 451.09461. Anal. calcd for C<sub>29</sub>H<sub>16</sub>O<sub>4</sub>: C, 81.30; H, 3.76%. Found: C, 81.23; H, 3.70%.

3-(4-Isopropylphenyl)-2-(2-naphthylcarbonyl)-4,9-dihydronaphtho[2,3-b]furane-4,9-dione (10m). Yellow solid; Yield: 78% (MW), 70% (Thermal); m.p. 170-171 °C; IR (KBr): 1743, 1683, 1544, 1359, 1267 cm<sup>-1</sup>; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta_{\rm H}$ : 1.11 (d, 6H, J = 6.9, CH<sub>3</sub>), 2.80 (sep, 1H, J = 6.9, CH), 7.13 (d, 2H, J = 8.4, Ar–H), 7.41 (d, 2H, J = 8.1, Ar–H), 7.50 (t, 1H, J = 7.5 Hz, Ar–H), 7.59 (t, 1H, J = 7.5, Ar–H), 7.79–7.84 (m, 5H, Ar–H), 7.90 (dd, 1H, J = 8.7, 1.5 Hz, Ar–H), 8.17–8.21 (m, 1H, Ar-H), 8.27-8.30 (m, 1H, Ar-H), 8.33 (s, 1H, Ar-H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta_{\rm C}$ : 23.6, 33.9, 124.7, 125.5, 126.0, 126.7, 126.9, 127.3, 127.7, 127.8, 128.4, 128.8, 129.7, 130.3, 132.0, 132.2, 132.4, 132.5, 133.0, 134.0, 134.4, 135.7, 149.9, 150.9, 152.7, 174.1, 180.1, 183.9. HRMS (positive ESI): m/z calcd for C<sub>32</sub>H<sub>22</sub>O<sub>4</sub> + Na<sup>+</sup>: 493.14158. Found: 493.14103. Anal. calcd for C32H22O4: C, 81.69; H, 4.71%. Found: C, 81.62; H, 4.65%.

**3-(4-Chlorophenyl)-2-(2-naphthylcarbonyl)-4,9-dihydronaphtho**[2,3-*b*]**furan-4,9-dione (10n).** Yellow solid; Yield: 81% (MW), 74% (Thermal); m.p. 203–204 °C; IR (KBr): 1741, 1661, 1639, 1351, 1218 cm<sup>-1</sup>; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta_{\rm H}$ : 7.35–7.38 (m, 2H, Ar–H), 7.48–7.53 (m, 2H, Ar–H), 7.55–7.66 (m, 2H, Ar–H), 7.78–7.84 (m, 2H, Ar–H), 7.86–7.91 (m, 2H, Ar–H), 7.94–8.00 (m, 2H, Ar–H), 8.15–8.19 (m, 1H, Ar–H), 8.24–8.30 (m, 1H, Ar–H), 8.50 (s, 1H, Ar–H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta_{\rm C}$ : 124.7, 126.8, 126.9, 127.0, 127.3, 127.7, 127.8, 128.2, 128.6, 129.1, 129.8, 130.7, 131.6, 132.3, 132.6, 133.1, 133.7, 134.1, 134.5, 135.3, 135.9, 150.9, 152.4, 173.9, 179.9, 183.3. HRMS (positive ESI): m/z calcd for C<sub>29</sub>H<sub>15</sub>ClO<sub>4</sub> + Na<sup>+</sup>: 485.05566 (M<sup>+</sup>), 487.05271 (M + 2)<sup>+</sup>. Found: 485.05511, 487.05216. Anal. calcd for C<sub>29</sub>H<sub>15</sub>ClO<sub>4</sub>: C, 75.25; H, 3.27%. Found: C, 75.19; H, 3.33%.

**3-(3-Fluorophenyl)-2-(2-naphthylcarbonyl)-4,9-dihydronaphtho[2,3-***b***]<b>furan-4,9-dione (100).** Yellow solid; Yield: 77% (MW), 71% (Thermal); m.p. 179–180 °C; IR (KBr): 1670, 1661, 1639, 1359, 1267 cm<sup>-1</sup>,'H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta_{\rm H}$ : 7.02– 7.08 (m, 1H, Ar–H), 7.30–7.34 (m, 3H, Ar–H), 7.56 (t, 1H, J = 7.5, Ar–H), 7.64 (t, 1H, J = 7.5, Ar–H), 7.81–8.00 (m, 6H, Ar–H), 8.18–8.21 (m, 1H, Ar–H), 8.28–8.31 (m, 1H, Ar–H), 8.48 (s, 1H, Ar–H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta_{\rm C}$ : 116.4, 117.6, 117.9, 125.1, 126.4, 127.3, 127.7, 128.2, 129.0, 129.5, 129.8, 129.9, 130.2, 130.7, 130.9, 132.9, 133.5, 134.2, 134.5, 134.9, 136.3, 141.4, 152.8, 162.6, 174.3, 180.2, 183.7. HRMS (positive ESI): *m/z* calcd for C<sub>29</sub>H<sub>15</sub>FO<sub>4</sub> + Na<sup>+</sup>: 469.08521 (M<sup>+</sup>). Found: 469.08466. Anal. calcd for C<sub>29</sub>H<sub>15</sub>FO<sub>4</sub>: C, 78.02; H, 3.39%. Found: C, 77.94; H, 3.33%.

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